

Appl. No. : 09/866,034  
Filed : May 25, 2001

## REMARKS

Following Applicants' response to the Final Office Action, filed on May 19, 2003, the Examiner issued an Advisory Action on July 3, 2003, in which she indicated that rejections of the claims under 35 U.S.C. § 112, second paragraph, and objections to the misnumbering of the tables have been overcome. However, the Examiner maintained that all of the pending claims remain rejected, presumably under 35 U.S.C. §§ 101 and 112, first paragraph.

The Examiner cites Heid et al., submitted by Applicants as Appendix D of the Goddard Declaration filed with the Response of May 19, 2003, and notes that the data provided in Heid provides the standard deviations for calculating the Ct values, whereas the present specification does not provide the standard deviations for  $\Delta$ Ct. The Examiner states that

Note that contrary to the presentation of data in the specification as originally filed, the standard in the art as evidenced by page 990 of Heid et al. is to furnish both mean and standard deviation values. Thus, although this type of assay may be used in the art, the data presented in the specification are not sufficient to support applicants' assertions of utility for cancer diagnosis, and applicants have not furnished facts or evidence to the contrary.

Thus, this aspect of the Examiner's comments imply that while Applicants' assertion of utility is in fact substantial and specific ("this type of assay may be used in the art" and "utility for cancer diagnosis"), the utility is allegedly not credible for want of data that furnishes both mean and standard deviation values.

Applicants respectfully traverse. An Applicant's assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility requirement of 35 U.S.C. § 101, "unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope." *In re Langer*, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA 1974). See, also *In re Jolles*, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980); *In re Irons*, 340 F.2d 974, 144 USPQ 351 (1965); *In re Sichert*, 566 F.2d 1154, 1159, 196 USPQ 209, 212-13 (CCPA 1977). Compliance with 35 U.S.C. § 101 is a question of fact. *Raytheon v. Roper*, 724 F.2d 951, 956, 220 USPQ 592, 596 (Fed. Cir. 1983) cert. denied, 469 US 835 (1984). The evidentiary standard to be used throughout *ex parte* examination in setting forth a rejection is a preponderance of the totality of the evidence under consideration. *In re Oetiker*, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992) Thus, to overcome the presumption of truth that an assertion of utility by the applicant enjoys, the Examiner must establish that it is more likely than not that one of ordinary

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skill in the art would doubt the truth of the statement of utility. In other words, "Office personnel must provide evidence sufficient to show that the statement of asserted utility would be considered 'false' by a person of ordinary skill in the art." M.P.E.P. 2107.2(III)(A), February 2003, page 2100-38. Furthermore, "An assertion is credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based are inconsistent with the logic underlying the assertion." Id. at 2107.2(III)(B), page 2100-40.

Applicants respectfully submit that the Examiner has not met this burden. The specification indicates that TaqMan<sup>TM</sup> 5' nuclease assay was used in obtaining the Ct and  $\Delta$ Ct values reported in the specification. The Goddard Declaration clearly indicates that "the TaqMan<sup>TM</sup> PCR assay is described, for example, in the following scientific publications: . . . Heid et al. . . ." Goddard Declaration, paragraph 5.

Thus, evidence of asserted utility presented in the present application irrefutably provides that data was collected according to the established procedures in the art, that the Ct values obtained were in fact above the noise level of the background, and that the  $\Delta$ Ct values are in fact significantly above standard deviation in the Ct values. The Examiner has not provided any evidence to show that that these statements are false and that the Applicants did not follow the procedures acceptable in the art in general, and set forth in Heid et al. specifically. Accordingly, Applicants respectfully maintain barring any evidence to the contrary, and following the directions of M.P.E.P., the Examiner must find Applicants' assertions as true and find credible utility.

In addition, Applicants respectfully submit that the Examiner has not challenged the logic of the asserted utility. In fact, the Examiner has indicated that "this type of assay may be used in the art." Applicants further maintain that the facts presented in the specification and the Goddard Declaration are consistent with the logic of the asserted utility. The Examiner has required that the data collected be consistent with the art-accepted methodology. The Goddard Declaration clearly sets out that the TaqMan<sup>TM</sup> PCR assay identified in the specification was used according to the teachings of the art, including Heid et al. Accordingly, Applicants respectfully maintain that since the two criteria for lack of credible utility set forth in M.P.E.P. 2107.2(III)(B) are not met, the asserted utility is credible.

The Examiner then restates her previous objections that the present invention does not account for the aneuploidy of cancer cells. Applicants respectfully traverse.

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Enclosed herewith as Exhibit A is a Declaration by Avi Ashkenazi, Ph.D., an expert in the field of cancer biology and an inventor of the present application. This declaration was submitted in a co-owned U.S. Application Serial No. 09/903,925. As Dr Ashkenazi explains,

An increase in gene copy number can result not only from intrachromosomal changes but also from chromosomal aneuploidy. It is important to understand that detection of gene amplification can be used for cancer diagnosis even if the determination includes measurement of chromosomal aneuploidy. Indeed, as long as a significant difference relative to normal tissue is detected, it is irrelevant if the signal originates from an increase in the number of gene copies per chromosome and/or an abnormal number of chromosomes. (Emphasis provided.)

Ashkenazi Declaration, paragraph 5. Thus, as Dr. Ashkenazi explains, whether or not the cells exhibit aneuploidy, the presently claimed polypeptides can be used to determine whether overexpression of certain genes occurs in a cell, and thereby detect whether or not the cell is cancerous. Accordingly, Applicants respectfully maintain that the possible aneuploidy of cancer cells is irrelevant in the use of the proteins of the present invention in detecting cancerous cells.

Lastly, the Examiner has found Applicants' argument at page 5, first full paragraph of the Response of May 19, 2003 to confuse the issues. Applicants regret the confusion and set out to clarify the point further. The cited paragraph was meant to demonstrate that Applicants view a  $\Delta C_t$  value of 1 to be significant. This value is the threshold value that determines whether a test sample will be submitted for further analysis to determine whether it is in fact cancerous, or whether the test sample will be considered to be normal. The paragraph does not discuss pre-selection, nor does it suggest that the samples should be pre-selected.

In view of the above, Applicants respectfully submit that the assertion of utility is substantial, specific, and credible. Accordingly, Applicants respectfully request that the rejections based on 35 U.S.C. §§ 101 and 112, first paragraph, be withdrawn.

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CONCLUSION

Applicants respectfully maintain that claims are patentable and request that they be passed to issue. Applicants have submitted herewith a check in the amount of \$770 to cover the fee for the Request for Continued Examination. If this fee is incorrect, please charge any additional fees, including any fees for any extensions of time, or credit overpayment to Deposit Account No. 11-1410. Applicants invite the Examiner to call the undersigned if any issues may be resolved through a telephonic conversation.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 11/3/03

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